REMARKS

Status of the Claims

Claims 1, 32-34, 39-45, 50-52, 57-61, and 63-70 are currently pending and under examination in the present application. Claims 2-31, 35-38, 46-49, 53-56, and 62 have been canceled without prejudice or disclaimer of the subject matter claimed therein.

Amendments to the Claims

Claims 1, 32-34, 39, 50, 58, and 59 have been amended. The amendments to claims 1, 32-34, 39, 50, 58, and 59 do not introduce prohibited new matter.

Support for the amendments to claims 1, 50, 58, and 59 can be found throughout the specification. Representative support can be found at paragraph 0074, lines 4-7. Representative support for the amendments to claims 1 and 59 can also be found in claim 2 as originally filed.

Claims 32-34 and 39 have been amended to correct the dependency of the claims since claim 2 has been canceled.

New claims 69 and 70 have been added. Representative support for claims 69 and 70 can be found at paragraph 0011, lines 3-5. New claims 69 and 70 do not introduce prohibited new matter.

Rejection Under 35 U.S.C. 112, First Paragraph

Claims 1-3, 32-34, 37-55, and 57-68 are rejected under 35 U.S.C. § 112, first paragraph, because the Office Action alleges that the specification does not enable a method of removing amyloid deposits from a subject comprising administering to the subject any amyloid fibril or a pharmaceutical composition formulated for removing amyloid deposits from a subject comprising any amyloid fibrils.

Without acquiescing to the propriety of this rejection, the claims have been amended. The currently pending claims, including new claims 69 and 70, are directed to methods of removing amyloid deposits from a subject comprising administering to the subject amyloid fibrils comprising immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide, heterologous to the amyloid fibrils in the subject, in an effective amount to generate

an immune response. The currently pending claims are also directed to pharmaceutical compositions comprising an effective amount of amyloid fibrils for removing amyloid deposits from a subject, wherein the amyloid fibrils comprise immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide, heterologous to the amyloid fibrils in the subject.

Applicants respectfully point out that the initial burden is on the Examiner to provide a reasonable explanation as to why the scope of protection provided by the claim is not adequately enabled by the disclosure. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Moreover, the court in *In re Marzocchi* stated that it is incumbent upon the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Office Action has not provided any reason to doubt the enablement of the claimed invention. Moreover, the Office Action has not provided a reasonable explanation or evidence establishing the nonenablement of the claims. In the absence of evidence to the contrary, the specification fully enables the claims directed to a method of removing amyloid deposits from a subject comprising administering to the subject amyloid fibrils comprising immunoglobulin light chain polypeptide, heterologous to the amyloid fibrils in the subject, in an effective amount to generate an immune response, wherein the amyloid fibrils do not comprise amyloid β-protein.

The Office Action alleges that the specification only provides cursory conclusions without data supporting the findings. As discussed in the response submitted June 19, 2006, Applicants respectfully point out that Example D on page 35 discloses data supporting the removal of amyloid deposits from mice. Moreover, the specification describes the use of amyloid fibrils heterologous to the amyloid fibrils in the subject to treat subjects having amyloid deposits (paragraph 0074, lines 1-4 and paragraph 0132). Also, the reference of Schell (Schell *et al.* Prevention of AA Amyloidosis by Active Immunotherapy. Amyloid and Amyloidosis 2001. Miklos Bely and Agnes Apathy Eds. Agnes Apathy Publishing, Budapest, pp.234-235), submitted with the response of June 19, 2006, confirms that amyloid fibrils heterologous to the amyloid fibrils in the amyloid deposits of a subject can remove the amyloid deposits from the subject. Specifically, Schell shows that amyloid fibrils obtained from light chain

immunoglobulin are capable of removing amyloid deposits in AA-amyloidotic mice. The amyloid fibrils administered to the subject are heterologous to the amyloid fibrils in the amyloid deposits of a subject in terms of the precursor proteins from which they are derived. Likewise, Wall shows that the mAb 11-1F4 expedited the removal of systemic AA amyloid deposits, composed of serum amyloid protein A in a murine model of inflammation-associated amyloidosis (Wall *et al.*, 2001, Amyloid and Amyloidosis: Proceedings of the IXth International Symposium on Amyloidosis, Budapest, Hungary, David Apathy, submitted with the response of July 14, 2003). As discussed in the previous response, mAb 11-1F4 was generated using, as an immunogen, the heat aggregated fibrillar form of a human V_L fragment obtained from proteolytic cleavage of the human κ4 immunoglobulin light chain protein LEN. Both Schell and Wall support the presently claimed invention.

Applicants respectfully point out that the references of Schell and Wall are provided to support the enablement of the claims by the specification. The specification describes and enables the use of amyloid fibrils to remove amyloid deposits in a subject (paragraphs 0128-0133). As an example, the specification describes in detail the use of immunoglobulin light chain polypeptide to remove amyloid deposits from mice with reduced AL-amyloidoma and AA-amyloidosis (paragraphs 0128-0131). Immunoglobulin light chain polypeptide is structurally, and functionally heterologous to the serum amyloid protein A that comprises the amyloid fibrils in mice induced to develop AA-amyloidosis. The specification, in paragraphs 0132 and 0133, further discusses in detail the use of amyloid fibrils heterologous to the amyloid fibrils in the subject to remove amyloid deposits from the subject. Accordingly, the references Schell and Wall confirm what the specification already teaches and enables.

The Office Action alleges that the claimed invention requires undue experimentation based on the Wands factors. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). However, Applicants respectfully point out that the factors have been considered with respect to the enablement issue and that it would not require undue experimentation to practice the claimed invention for reasons discussed below.

The claimed methods as they stand are directed to a method of using amyloid fibrils comprising immunoglobulin light chain polypeptide or whole immunoglobulin light chain

polypeptide, heterologous to the amyloid fibrils in the subject, for removing amyloid deposits from the subject. The claims are not directed to the use of any amyloid fibrils for removing amyloid deposits from a subject.

As discussed above, the specification describes in detail the claimed invention and provides working examples of the claimed method. As stated in the MPEP (2164.02), an applicant need not have actually reduced the invention to practice prior to filing. *Gould v. Quigg,* 822 F.wd 1074, 1078 (Fed. Cir. 1987). Further, the MPEP (2164.02) states that the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908 (CCPA 1970). Since the specification describes the claimed invention in detail and provides working examples of the claimed method, the specification also provides sufficient guidance or direction to enable the claimed invention. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *Id.* Moreover, the court explained that an extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance. *In re Colianni*, 561 F.2d 220, 224 (CCPA 1977).

Regarding the state of the prior art, the nature of the invention, the relative skill of those in the art, and the unpredictability of the art, the specification teaches the use of amyloid fibrils heterologous to the amyloid fibrils in the subject to remove amyloid deposits from the subject. Moreover, Applicants have provided the references of Schell and Wall as proof of enablement of the scope of the invention. Thus, given the state of the prior art, the supporting evidence provided by Applicants, and the teachings and guidance from the specification, a person of ordinary skill in the art would be able to practice the claimed invention without undue experimentation. Accordingly, the specification enables the scope of the claims.

Further new claims 69 and 70 are directed to a method of using immunoglobulin light chain polypeptide comprising the κ or λ chain. As discussed in paragraph 0011 of the specification, the κ and λ chains of immunoglobulin light chain polypeptide are not structurally homologous molecules. They have different amino acid sequences. Hrncic (Hrncic *et al.* Am J. Path. 2000 157(4):1239, submitted with response of July 14, 2003) show that mAb 11-1F4,

generated using as an immunogen, κ4 immunoglobulin light chain protein, combined with an adjuvant, was able to remove ALλ amyloidoma. Accordingly, Hrncic confirms what is taught by the specification.

Accordingly, the specification enables the scope of the claims.

Rejection Under 35 U.S.C. § 102(e)

Claims 1, 2, 32-34, 37-45, 50-52, 57-61 and 63-68 are rejected under 35 U.S.C. 102(e) as being anticipated by Schenk (U.S. Patent 6,875,434).

Without acquiescing to the propriety of the rejection, the claims have been amended. The currently pending claims, including new claims 69 and 70, are directed to a method of removing amyloid deposits from a subject comprising administering to the subject amyloid fibrils comprising immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide, heterologous to the amyloid fibrils in the subject, in an effective amount to generate an immune response. The currently pending claims are also directed to pharmaceutical compositions comprising an effective amount of amyloid fibrils for removing amyloid deposits from a subject, wherein the amyloid fibrils comprise immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide, heterologous to the amyloid fibrils in the subject.

Schenk does not disclose or suggest the use of amyloid fibrils that are heterologous to the amyloid fibrils in the subject for removing amyloid deposits from a subject. Rather, Schenk is focused on administering amyloid fibrils that are homologous to the amyloid fibrils in the subject to remove amyloid deposits (see col. 6, line 65 to col. 19). The Examples of Schenk only disclose the use of Aβ peptides or fragments thereof for removing Aβ deposits from subjects such as PDAPP mice. The claims of Schenk are limited to the use of Aβ fragment to treat Alzheimer's disease. Accordingly, Schenk does not disclose or suggest the use of amyloid fibrils heterologous to the amyloid fibrils in a subject for removing amyloid deposits. Therefore, Schenk does not anticipate the claimed invention.

Rejection Under 35 U.S.C. 102(a)

Claims 1, 32-34, 37-45, 57, 59, and 64-68 are rejected under 35 U.S.C. 102(a) as being anticipated by Schenk (WO 99/27944).

As discussed above, the claims have been amended. The currently pending claims are directed to a method of using amyloid fibrils comprising immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide, heterologous to the amyloid fibrils in the subject, in an effective amount to generate an immune response for removing amyloid deposits from a subject. The currently pending claims also are directed to pharmaceutical compositions comprising the amyloid fibrils amyloid fibrils comprising immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide, heterologous to the amyloid fibrils in the subject, in an effective amount to generate an immune response for removing amyloid deposits from a subject.

The cited reference, Schenk, does not disclose or suggest administering amyloid fibrils composed of immunoglobulin light chain polypeptide or whole immunoglobulin light chain polypeptide to a subject for removal amyloid deposits from the subject. Moreover, Schenk does not teach administering amyloid fibrils that are heterologous to the amyloid fibrils in the subject. Schenk only discloses administering Aβ peptide or fragments thereof to treat patients suffering from Alzheimer's disease. Aβ peptide or fragments are homologous to the amyloid fibrils in patients suffering from Alzheimer's disease. Accordingly, Schenk does not anticipate the claimed invention.

Conclusion

In view of the foregoing claim amendments and accompanying remarks, Applicants respectfully request reconsideration and timely allowance of the pending claims. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact Applicants' undersigned representative to expedite prosecution.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
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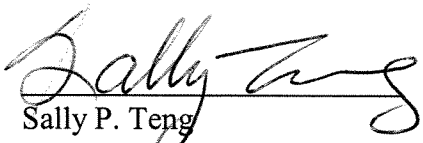

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